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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,143	11/03/2003	Robert M. Lorence	18029	3847

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EXAMINER	
KINSEY, NICOLE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/700,143	LORENCE ET AL.	
	Examiner	Art Unit	
	Nicole E. Kinsey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/6/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/04, 7/8/04 and 12/8/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-23 are pending and under examination.

Priority

Claims 1-21 have written description support in provisional application 60/423,952 (11/5/2002). Therefore, claims 1-21 have a priority date of 11/5/2002.

Claims 22 and 23 do not have written description support in provisional application 60/423,952 (11/5/2002). Although Example I of this application discloses that the patient had been administered octreotide, this example does not disclose that after treatment with NDV, her octreotide dose was reduced or eliminated. Provisional application 60/457,034 (3/24/2003), however, does disclose that patient 2102 of Example 2 was taken off octreotide after treatment with NDV. Therefore, claims 22 and 23 have a priority date of 3/24/2003.

Information Disclosure Statement

The information disclosure statements submitted 3/4/2004, 7/8/2004, 12/8/2004 and 7/6/2005 have been considered by the Examiner.

Specification

The use of the trademark SANDOSTATIN has been noted in this application on page 5. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the condition" and Claim 9 recites "the dose." Further, claim 22 recites "the therapeutic virus treatment." There is insufficient antecedent basis for these limitations in the claims.

Claim 23 is unclear. Claim 20, from which claim 23 depends, requires i) the presence of carcinoid syndrome (one or both of diarrhea and flushing symptoms), ii) administration of octreotide to control the diarrhea or flushing before administration of the virus, iii) administering the virus, and iv) a decrease in the carcinoid symptom is measured by a decrease in the dose of octreotide needed to control the symptom.

If the symptom is not controlled by octreotide as recited in claim 23, then step ii) above, which requires the administration of octreotide to control the symptom, is no longer necessary. This then makes step iv), which requires a measurement of octreotide, impossible to perform because there was no octreotide administered. If Applicants meant to eliminate steps ii) and iv), then the claim makes no sense. If, in the alternative, Applicants mean that the subject was treated with octreotide before administration of the virus, and after administration of the virus, the subject no longer needed any octreotide to control the carcinoid symptom, then the claim needs to be clarified to state this.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 7, and 16-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a carcinoid tumor with the mesogenic strain MK107 of Newcastle Disease Virus (NDV), does not reasonably provide enablement for any negative-stranded RNA virus, any replication-competent oncolytic virus, any Paramyxovirus, any strain of NDV or any mesogenic NDV strain other than MK107. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Scope of enablement is considered in view of the Wands factors (MPEP 2164.01(a)).

Nature of the invention. The claims are drawn to a method of treating a carcinoid tumor by administering a negative-stranded RNA virus to a mammal.

State of the prior art. At the time the invention was made, only certain NDV strains were labeled as "antineoplastic agents" for human tumors (See Sinkovics et al.). In addition, Sinkovics et al. states that "[v]arious NDV strains differ widely in their biological effects including oncolysis and without specific studies of a given NDV strain, generalizations that it is oncolytic just because it is a NDV strain are invalid and unacceptable." (See Sinkovics et al. entire article, especially page 11). Furthermore, Wildner states, with respect to NDV, that "[s]train differences are substantial in respect to virulence, syncytium formation, replication, immune response, and oncolysis (See Wildner at pages 297-297, Newcastle disease virus heading).

Breadth of the claims. The claims are extremely broad, encompassing treatment of a carcinoid tumor with any negative-stranded RNA virus, any replication-competent oncolytic virus, any Paramyxovirus, and any strain of NDV.

Working examples. There are only working examples for the mesogenic strain MK107 of NDV.

Guidance in the specification. The specification teaches only the use of the mesogenic strain MK107 of NDV to treat a carcinoid tumor. There is no specific guidance regarding administering to a mammal any other negative-stranded RNA virus, replication-competent oncolytic virus, Paramyxovirus, strain of NDV or mesogenic NDV strains other than MK107 to treat a carcinoid tumor.

Predictability of the art. The art with regard to NDV strains being oncolytic is acknowledged to be unpredictable as stated above under the heading *State of the prior art*. In the instant application, Applicants have not disclosed any other virus except the mesogenic MK107 strain of NDV, stating "[a]ny conventional negative-stranded RNA virus can be utilized in accordance with the invention to treat a mammalian subject having a carcinoid tumor." Ebola, Marburg and Reston viruses are negative-stranded RNA viruses of the family Filoviridae, which are not known to be oncolytic or to be useful for treating a carcinoid tumor.

Amount of experimentation necessary. It is not known whether other negative-stranded viruses, Paramyxoviruses, NDVs or mesogenic strains of NDV would have any effect against a carcinoid tumor.

It appears that Applicants have only disclosed one example of a particular species belonging to the genus mesogenic, but essentially all of the work required to identify other viruses as listed above has been left for others.

Claims must be commensurate in scope with the specification and one example is not enabling for the use of the class or genus of NDVs. In ex parte Jackson, 217 USPQ 805, even a "description of several newly discovered strains of bacteria having one particularly desirable metabolic property in terms of conventionally measured culture characteristics and number of metabolic and physiological properties does not enable one of ordinary skill in the relevant art to independently discover additional strains having the same specific, desirable metabolic property". Thus, the degree of experimentation involved in locating other NDVs, Paramyxoviruses, and negative-

stranded RNA viruses, etc., which would function in the claimed methods is undue in light of enablement requirement of 35 USC 112. The results achieved in the examples are not predictive of the effect of any mesogenic NDV, any NDV, any Paramyxovirus, or any negative-stranded RNA virus on a carcinoid tumor as claimed.

Given the breadth of the claims, the lack of guidance in the specification, and the predictability of the art, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-8, 13, 14 and 16-18 are rejected under 35 U.S.C. 102(a) as being anticipated by Pecora et al. as evidenced by Laurie et al.

Pecora et al. teaches that oncolytic NDV strains, including replication-competent PV701, administered intravenously (i.e., systemically), replicate selectively in human cancer cells implanted in athymic mice resulting in tumor regression (page 2251-introduction). Human patients with various tumor types (e.g., colorectal, pancreatic, renal, breast, lung, etc.) were also given PV701, which is mesogenic as evidence by Laurie et al. (page 2556 under heading Patients and Methods). The virus can be administered over one or more cycles where at least one cycle comprises one or more desensitizing does followed by one or more escalating does of a higher amount of virus (pages 2252-top of left column and 2253-under heading Desensitizing regimen). The desensitizing dose given was 1.2×10^{10} PFU per square meter of patient surface area and the escalating dose given was 2.4×10^{10}, 4.8×10^{10}, 7.2×10^{10}, 9.6×10^{10} or 1.44×10^{11} PFU per square meter of patient surface area (page 2253-under heading Desensitizing regimen).

Claims 22 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by the 9th Annual Ottawa Life Sciences International Conference and Exhibition (November 4-6, 2002).

The 9th Annual Ottawa Life Sciences International Conference and Exhibition discloses treating a mammalian subject having a carcinoid tumor, comprising administering to the subject an amount of a therapeutic virus (mesogenic strain PK701

of NDV) effective to treat the condition, wherein the virus is a negative-stranded RNA virus. It is also disclosed that the symptom of carcinoid syndrome comprises one or both of diarrhea and flushing, and before beginning the therapeutic virus treatment, octreotide was administered to the patient to control the symptom and the decrease in the symptom of carcinoid syndrome is measured by a decrease in the dose of octreotide needed to control the symptom (See entire presentation, especially page 10-top slide-Patient #2102). For patient #2102, octreotide was discontinued after administration of NDV, i.e., there was a decrease in the dose of octreotide needed to control the symptom. In addition, the patient's carcinoid syndrome (fatigue and diarrhea) was under control for over 3 months without administering octreotide.

Claims 1-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Roberts et al. (WO 00/62735) as evidenced by Chandler et al., Martensson et al., Drougas et al. and Wessels et al.

Roberts et al. teaches a method of treating a neoplasm, which is defined to include tumors and cancer, in a mammal by administering a replication-competent RNA virus (page 7, lines 4-8; pages 31-32; and Examples). Roberts et al. also discloses using a mesogenic strain of NDV (MK107) that selectively kills tumor cells (page 17, line 24 to page 18, line 26 and the Examples, especially Example 15). NDV is a Paramyxovirus (page 18, lines 6-15). The virus can be administered systemically or intravenously (page 33, lines 17 and 26), and the virus can be administered over the course of 4 minutes to 24 hours or 20 to 60 minutes (page 36, lines 16-19). The virus

can be administered over one or more cycles where at least one cycle comprises one or more desensitizing doses followed by one or more escalating doses of a higher amount of virus (pages 34-35 and the Examples, especially Example 20). The desensitizing dose can be at least 1.2×10^{10} PFU per square meter of patient surface area (page 35, line 17) and the escalating dose can be at least 2.4×10^{10} PFU per square meter of patient surface area (page 35, line 20). The subject can be human (page 65 and Example 20) or non-human (Examples 2-9), and after treating the subject, the size of the tumor decreases (page 32, lines 18-22 and Example 20).

Regarding claims 19 and 20, it is well known in the art that carcinoid tumors cause carcinoid syndrome. It is also well know that treating or reducing the size of the tumor by surgery, chemotherapy, radiofrequency ablation or chemoembolization results in a decrease or elimination of carcinoid syndrome as evidenced by Chandler et al., Martensson et al., Drougas et al. and Wessels et al. Patients who were taking octreotide before tumor treatment to control carcinoid syndrome were able to reduce their octreotide dose or eliminate their octreotide dose after tumor treatment (see Wessels et al. abstract). Further, a reduction of tumor size or eliminating the tumors also reduced the levels of 5-hydroxyindole acetic acid (5-HIAA) in urine (see Martensson et al., abstract). Therefore, a person of ordinary skill in the art would recognize that treating carcinoid tumors with other methods, including NDV, to reduce the size of or eliminate the tumors will inherently reduce or treat carcinoid syndrome, reduce the levels of 5-HIAA in urine, and reduce the need for octreotide.

Claims 1-8, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lorence et al. (WO 94/25627).

Lorence et al. teaches a method of treating cancer and tumors in a mammal by administering an effective amount of virus, which is a Paramyxovirus, preferably NDV (page 3, line 32 to page 4, line 2). "Cancer" is defined as the physiological condition in mammals that is usually characterized by unregulated cell growth. Thus, a carcinoid tumor is included. The virus specifically distinguishes mammalian cancer cells from normal cells and it is cytolytic (page 6, lines 15-25). Lorence et al. also discloses using a mesogenic strain of NDV (MK107) to treat tumors in athymic mice (Example 3). The virus can be administered systemically or intravenously (page 11, lines 20-25). The subject can be non-human (Examples 1-3), and after treating the subject, the size of the tumor decreases (Example 1).

Claims 1-4, 6, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Phuangsab et al.

Phuangsab et al. teaches a method of treating MM17387 colon tumors (adenocarcinoma) transplanted in athymic mice by administering the avian Paramyxovirus NDV replication-competent, strain 73-T to athymic mice (pages 27-28). The virus specifically distinguishes mammalian cancer cells from normal cells, and it is cytolytic (page 28, left column and Discussion). Phuangsab et al. also discloses that the virus can be administered systemically (page 30-33), and after treating the subject, the size of the tumor decreases (pages 29-33).

Claims 1-4, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Reichard et al.

Reichard et al. teaches treating tumors in athymic mice by administering a replication-competent oncolytic strain (73-T) of NDV. The virus specifically distinguishes mammalian cancer cells from normal cells, and it is cytolytic to tumor cells (page 452, right column-Discussion). After treating the subject, the size of the tumor decreases (pages 450-452).

Claims 1-8, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Lorence et al. (US Patent No. 7,056,689).

Lorence et al. discloses a method of treating cancer and tumors in a mammal by administering an effective amount of virus, which is a Paramyxovirus, preferably NDV (col. 6, lines 4-11). "Cancer" is defined as the physiological condition in mammals that is usually characterized by unregulated cell growth (col. 6, lines 6-9). Thus, a carcinoid tumor is included. The virus specifically distinguishes mammalian cancer cells from normal cells, and it is cytolytic (col. 4, lines 26-36 and col. 6, lines 28-32). Lorence et al. also discloses using a mesogenic strain of NDV (MK107) to treat tumors in athymic mice (Example 3). The virus can be administered systemically or intravenously (col. 7, lines 3-7 and Example 2). The subject can be non-human (Example 1), and after treating the subject, the size of the tumor decreases (Example 1-3).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pecora et al.

Pecora et al. teaches a desensitizing dose of 1.2×10^{10} PFU per square meter of patient surface area and escalating doses of 2.4×10^{10}, 4.8×10^{10}, 7.2×10^{10}, 9.6×10^{10} or 1.44×10^{11} PFU per square meter of patient surface area (page 2253-under heading Desensitizing regimen). In addition, Pecora et al. teaches rates of administration of 1.2×10^{9} PFU per square meter of patient surface area per minute for doses of 1.2×10^{10} per square meter of patient surface area and a rate of 5×10^{9} PFU per square meter of patient surface area per minute for doses greater than 1.2×10^{10} per square meter of patient surface area.

It is well within the purview of one of ordinary skill in the art to optimize dosages as well as the administration times as recited in claims 9 and 10.

According to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

A particular parameter must first be recognized as a result-effective variable, i.e., a variable, which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the instant application, the doses and rates of Pecora et al. produced a recognized result (i.e., tumor regression). Therefore, determining other optimum or workable dosages and rates is routine experimentation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 16-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 6, 7, 19, 22-25 and 27 of US Patent No. 7,056,689 ("the '698 patent"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating cancer in a mammal by administering a negative-stranded RNA virus (NDV). The carcinoid tumor of the instant application is within the breadth of the term cancer, which is recited in the '689 patent claims.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 157-161, 163-170, 172, 174, 183, 196-219, and 230-232 of copending Application No. 09/958,809. Although the conflicting claims are not identical, they are not patentably distinct from

each other because both sets of claims are directed to infecting a tumor in a mammal with a virus comprising administering to said mammal an RNA virus, wherein said virus is administered as a first dose and one or more subsequent doses, and wherein the first dose is a desensitizing dose, to thereby infect said tumor (Treating a tumor in a mammal with an oncolytic virus will, at the same time, infect the tumor).

Claims 1-8, 13, 16, and 17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 6-8, 50, 51, 63-65, 69, 70, 73, 115-120, 132, 134, 136, and 144 of copending Application No. 10/167652 ("the '652 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating cancer by administering a replication competent, interferon sensitive clonal RNA virus to a mammal. The carcinoid tumor of the instant application is within the breadth of the term neoplasm, which is recited in the '652 application claims (see claims 7, 50 and 51). In addition, treating a neoplasm or tumor in a mammal with a virus will, at the same time, infect the neoplasm or tumor.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 12, 17, 21, 22, 26-28 and 34 of copending Application No. 10/518,732 ("the '732 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to administering a therapeutic negative-stranded RNA virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially one or more desensitization doses of the

virus followed by administering one or more escalated doses of the virus, wherein the amount of the virus in each of the one or more escalated doses is higher than the amount of virus in each of the desensitization doses. Although claims 13-15 of the instant application do not recite "the amount of the virus in the second and any subsequent desensitization dose is not less than the amount of the virus in the preceding desensitization dose," the scope of the '732 claims overlaps with claims 13-15 of the instant application.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10/547,654 ("the '654 application"). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to administering a therapeutic negative-stranded RNA virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially one or more desensitization doses of the virus followed by administering one or more escalated doses of the virus, wherein the amount of the virus in each escalated dose is higher than the amount of virus in each desensitization dose. Although claims 13-15 of the instant application do not recite a time period between the desensitizing dose and the escalated dose or a rate for administration, the scope of the '654 claims overlaps with claims 13-15 of the instant application.

Claims 13-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/548,057 ("the '057 application"). Although the conflicting

claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to administering a therapeutic negative-stranded RNA virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially one or more desensitization/initial doses of the virus followed by administering one or more escalated/subsequent doses of the virus, wherein the amount of the virus in each escalated dose is higher than the amount of virus in each desensitization dose.

Claims 1-8 and 16-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14, 17, 18, 21, 22, 33, 34, 36-39, and 41 of copending Application No. 11/441,201. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of treating cancer or a tumor by administering to a mammal a negative-stranded RNA virus.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on 8:00 am to 4:30 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Nicole Kinsey, PhD
Patent Examiner
Art Unit 1648

Bruce Campell

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